

FIGURE 1

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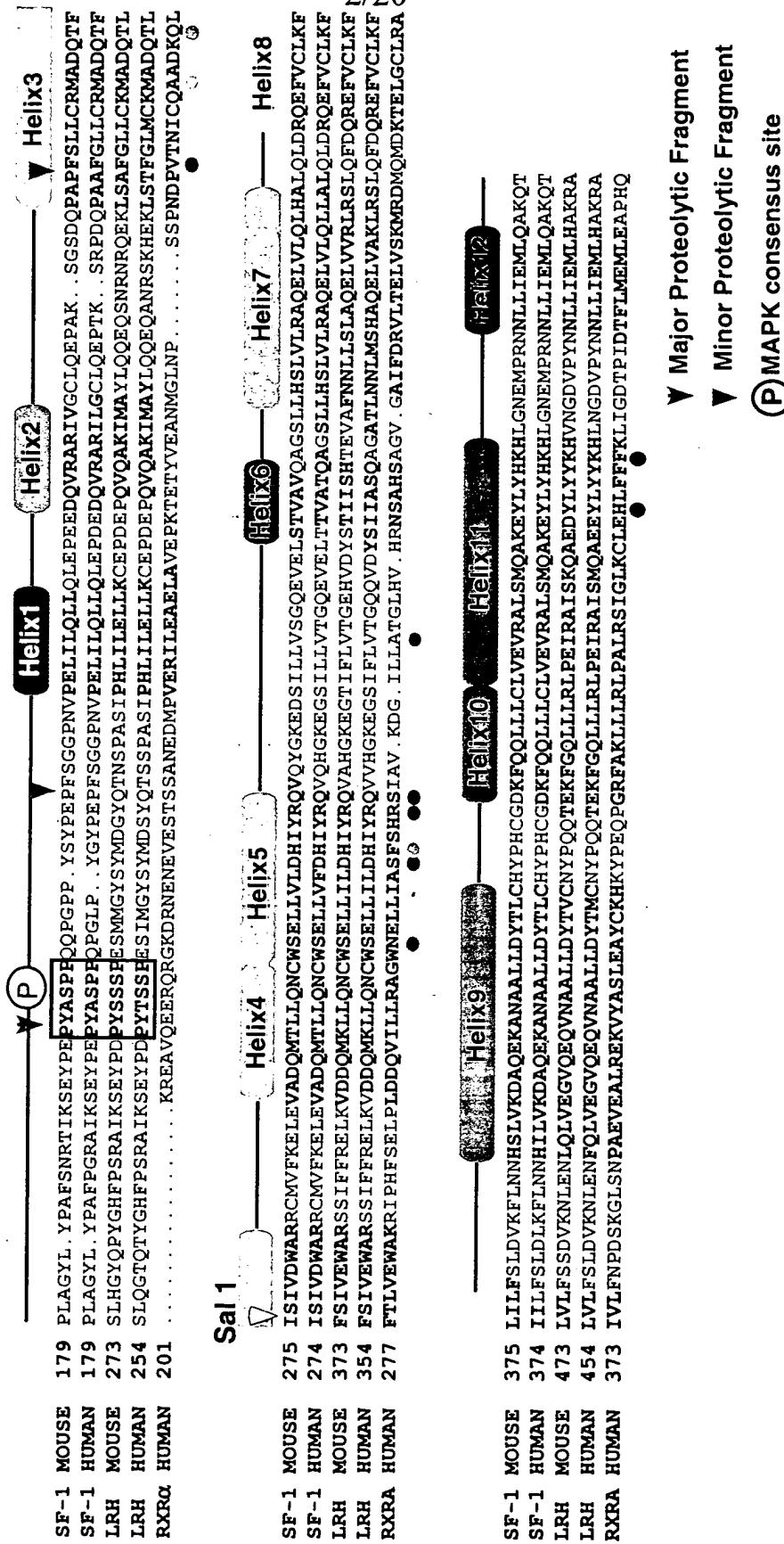


FIGURE 2

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A

1 atggactact cgtacgacga ggacctggac gagctgtgtc cagtgtgtgg tgacaaggta
61 tcgggctacc actacgggct gctcacgtgc gagagctgca agggcttctt caagcgcaca
121 gtccagaaca acaagcatta cacgtgcacc gagagtcaaga gctcaaaat cgacaagacg
181 cagcgttaagc gctgtccctt ctgcccgttc cagaagtgcc tgacgggtggg catgcgcctg
241 gaagctgtgc gtgctgatcg aatgcggggt ggccggaaca agtttgggccc catgtacaag
301 agagaccggg cttgaagca gcagaagaaa gcacagattc gggccaatgg cttcaagctg
361 gagaccggac caccgatggg ggtgcccccg ccaccccttc ccccacccgga ctacatgtta
421 cccccttagcc tgcacgcacc ggagcccaag gcccctggtct ctggcccacc cagtggccg
481 ctgggtgact ttggagcccc atctctaccc atggctgtgc ctggtcccca cggacactctg
541 gctggctacc tctatcctgc cttctctaac cgccaccatca agtctgagta tccagagccc
601 tatgccagcc ccccacacaaca gccaggccca ccctacagct atccagagcc cttctcagga
661 gggcccaatg taccagagct catattgcag ctgctgcaac tagagccaga ggaggaccag
721 gtgcgcgctc gcacgtggg ctgtctgcag gagccagcca aaagccgctc tgaccagcca
781 gcgccttca gcctcctctg cagaatggcc gaccagaccc ttatctccat tgtcactgg
841 gcacgaaggt gcatggtctt taaggagctg gaggtggctg accagatgac actgctgcag
901 aactgttgg a cgagctgct ggttggac cacatctacc gccaggtcca gtacgcga
961 gaagacagca tcctgctgg tactggacag gaggtggagc tgagcacagt ggctgtgcag
1021 gctggctccc tgctgcacag cctggctg cgggcccgg agttagtgct ccagtgcac
1081 gcaactgcaggc tggaccgcca ggagttcgctc tgtctcaagt tcctcatcct cttcagcctc
1141 gatgtgaaat tcctgaacaa ccacagcctc gtaaaggacg cccagggaaaa ggccaacgct
1201 gcccgttgg attacaccc ttgtcactac ccacactgcg gggacaaatt ccagcagttg
1261 ctattgtgcc tggtgaggt gcgggcccgg agcatgcagg ccaaggagta cctgtaccac
1321 aagcatttgg gcaacgagat gccccgcaac aacttctca ttgagatgct gcaggccaag
1381 cagacttga

B

MDYSYDEDLDELCPVCGDKVSGYHYGLLTCESCKGFFKRTVQNN
KHYTCTESQSKIDKTQRKRCFCRFQKCLTVGMRLEAVRADRMRGGRNKFGPMYKRD
RALKQQKKAQIRANGFKLETGPPMGVPPPPPPPDYMLPPSLHAPEPKALVSGPPSGP
LGDFGAPSLPMAVPGPGLAGYLYPAFSNRTIKSEYPEPYASPPQPGPPYSYPEPF
SGGPNVPELILQLLQLEPEEDQVRARIVGCLQEPAKSRSQDQPAPFSILLCRMADQTFIS
IVDWARRCMVFKELEVADQMTLLQNCWSELLVLDHIYRQVQYKGKEDSILLVTGQEVEL
STVAVQAGSLLHSLVLRQAELVQLHALQLDRQEFVCLKFLILFSLDVKFLNNHSLVK
DAQEKAANALLDYTLCHYPHCGDKFQQLLCLVEVRALSMQAKEYLYHKHGNEMPRN
NLLIEMLQAKQT

FIGURE 3

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A

1 gcgacgccc cgggcatgga ctattcgta gacgaggacc tggacgagct gtccccgtg
 61 tgcggggaca aggtgtccgg ctaccactac ggactgctca cgtgtgagag ctgcaagggc
 121 ttcttcaagc gcacggtgca gaacaacaag cactacacgt gcaccgagag ccagagctgc
 181 aagatcgaca agacgcagcg caagcgctgt cccttctgcc gcttccagaa atgcctgacg
 241 gtggggatgc gcctggaagc cgtgcgcgt gaccgtatga ggggtggccg gaacaagttt
 301 gggccgatgt acaagcgga ccgggcccgt aaacagcaga agaaggcaca gattcgggcc
 361 aatggcttca agctggagac agggcccccgt atgggggtgc ccccgccgccc ccctccgc
 421 ccggactacg tgctgcctcc cagcctgcat gggcctgagc ccaaggccct ggccggcggt
 481 ccacctgctg gccactggg cgactttggg gccccagcac tgcccatggc cgtccgggt
 541 gcccacgggc cactggctgg ctacctctac cctgccttc ctggccgtgc catcaagtct
 601 gagtacccgg agccttatgc cagccccca cagcctggc tgccgtacgg ctacccagag
 661 cccttctctg gaggccccaa cgtgcctgag ctcatcctgc agctgctgca gctggagccg
 721 gatgaggacc aggtgcgggc cgcacatctg ggctgcctgc aggagccac caaaagccgc
 781 cccgaccagc cggcggcctt cggcctcctg tgcagaatagg ccgaccagac cttcatctcc
 841 atcgtggact gggcacgcag gtgcatggc ttcaaggagc tggaggtggc cgaccagatg
 901 acgctgctgc agaactgctg gagcgagctg ctgggtttcg accacatcta ccgcaggc
 961 cagcacggca aggagggcag catcctgctg gtcaccgggc aggaggtgga gctgaccaca
 1021 gtggccaccc aggcggtc gctgctgcac agcctgggt tgccggcgca ggagctgggt
 1081 ctgcagctgc ttgcgtcga gctggaccgg caggagtttgc tctgcctcaa gttcatcatc
 1141 ctcttcagcc tggatttgaat gttcctgaat aaccacatcc tggtaaaaga cgctcaggag
 1201 aaggccaacg ccgcctgtct tgactacacc ctgtgccact acccgactg cggggacaaa
 1261 ttccagcagc tgctgtgtg cctggggag gtgcgggccc tgagcatgca gccaaggag
 1321 tacctgttacc acaagcacct gggcaacgcag atgccccgca acaacgtct catcgaaatg
 1381 ctgcaagccaa agcagactt gagectggcc gggggcgggg ccggactgg gggcggact
 1441 gggggcgggg cctggcggg gccgcagcca caccgctggc tccgcattgt tcatttctg
 1501 atgcccaccc aggagccccaa gccccgtccc agaggccgct gcccctgagt tctgacactg
 1561 tgggtttggg aagggtgggtg aggctggca gggcctggc gaggtggagt gcccactggc
 1621 actgcctgc tgcttggagt gccccaaagga ggtggctgtt aaccacccgc cccgccccct
 1681 ccctgctccc agctctctct cctggagtttctt gaagcctgca ggtccggga ggaggttcgg
 1741 gattccctgg tgggcctcga cgtcccttgg atcagaggtt atcccttctt cctctcttgg
 1801 aaacagacag ggagaagttt agcaggttata aactagggga ggagagaggg tctccagtgt
 1861 tccccccata gagaccagga gggagagcct ctgtt

B

MDYSYDEDLDELCPVCGDKVSGYHYGLLTCESCKGFFKRTVQNN
 KHYTCTESQSKIDKTQRKRCFCRFQKCLTVGMRLEAVRADMRGGRNKFGPMYKRD
 RALKQQKKAQIRANGFKLETGPPMGPVPPPPPAPDYVLPPSLHGPEPKGLAAGPPAGP
 LGDFGAPALPMAPVPGAHGPLAGYLYPAFPGRAIKSEYYPEPYASPPQPGPLPYGYPEPFS
 GGPNVPELILQLLQLEPDEDQVRARILGCLQEPTKSRPDQPAAFGLLCRMADQTFISI
 VDWARRCMVFKELEVADQMTLLQNCWSELLVFDHIYRQVQHGKEGSILLVTGQEVELT
 TVATQAGSLLHSLVLRAQELVLQLLALQLDRQEFVCLKFIILFSLDLKFLNNHILVKD
 AQEKANAALLDYTLCHYPHCGDKFQQLLCLVEVRALSMQAKELYHKHLGNEMPRNN
 LLIEMLQAKQT

FIGURE 4

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1 tttttttcc cccttttct taactttcac taaggaaatg agggttactg tagtctgagg
61 tttccttccc aaagtcacaa aatatgacaa gctgcaatct ttctcacatt caatgattc
121 tgctgttaagc caaaggactg ccaataattt cgctaagaat gtctgctagt ttggatactg
181 gagattttca agaatttctt aagcatggac ttacagctat tgcgtctgca ccagggtcag
241 agactcgcca ctcccccaaa cgtgaggaac aactccggga aaaacgtgt gggcttccgg
301 accgacacccg acgccccatt cccgccccca gccgccttgc catgctgccc aaagtggaga
361 cggaaagcccc aggactggtc cgatcgcatg gggAACAGGG gcagatgccaa gaaaacatgc
421 aagtgtctca atttaaaatg gtgaattact cctatgtat agatctggaa gagctatgtc
481 ctgtgtgtgg cgataaaatg tctgggtacc attacggtct ctcacgtgc gaaagctgca
541 agggttttt taagcgaact gtccaaaacc aaaaaaggta cacgtgcata gagaaccaga
601 attgccaaat tgacaaaaacg cagagaaaaac gatgtcccta ctgtcgattc aaaaaatgt
661 tcgatgttgg gatgaagctg gaagccgtaa gagccgaccg catgcgaggg ggcagaaata
721 agtttgggccc aatgtacaag agagacaggg ctttgaagca gcagaagaaa gcccattc
781 gagccaatgg acttaagctg gaagccatgt ctcaggtat ccaagcaatg ccctcagacc
841 tgacctctgc aattcagaac attcattccg cctccaaagg cttacctctg agccatgttag
901 ccttcctcc gacagactat gacagaagtc ctttgcac atctccatt agcatgacaa
961 tgcacccctca cagcagcctg catggttacc aaccctatgg tcactttct agtcgggcca
1021 tcaagtctga gtacccagac ccctactcca gtcacactga gtcaatgtat gttactcct
1081 acatggatgg ttaccagaca aactccccgg ccagcatccc acacctgata ctggacttt
1141 tgaagtgtga accagatgag cctcaagttc aagcgaagat catggcttac ctccagcaag
1201 agcagagtaa ccgaaacagg caagaaaagc tgagcgcatt tgggctttta tgaaaatgg
1261 cggaccagac cctgttctcc attgtttagt gggccaggag tagtatcttc ttcagggaa
1321 tgaaggttga tgaccaaatg aagctgcttc aaaactgctg gagtgagctc ttgattctcg
1381 atcacattta ccgacaatg gcgcatggga aggaaggag aatttcctg gttactggag
1441 aacacgtgga ctactccacc atcatctcac acacagaagt cgcgttcaac aacctctga
1501 gtctcgacca ggagctggg gtgaggctcc gttcccttca gttcgatcag cgggagttt
1561 tatgtctcaa gttcctggg ctgttcagct cagatgtgaa gaacctggag aacctgcac
1621 tgggaaagg tgtccaagag caggtgaatg ccgcctgtc ggactacacg gttgcaact
1681 acccacaaca gactgagaaa ttccggacagc tacttctcg gctaccggag atccggca
1741 tcagcaagca ggcagaagac tacctgtact ataaggacatg gaacggggat gtccctata
1801 ataacctcct cattgagatg ctgcacccca aaagagccta agtccccacc cctggaaagct
1861 tgctctagga acacagactg gaaggagaag aggaggacga tgacagaaac acaatactct
1921 gaactgctcc aagcaatgt aattataaaac ttggttaaa gacactgaat tttaaaagca
1981 taataattaa atacctaata gcaaataaat gatatatcag gttattgtt ctgcaactg
2041 tgaatcaaag gctgtatgaa tcaaaggatt catatgaaag acattgtat ggggtggatt
2101 gaacttacag atggagacca ataccacagc agaataaaaaa tggacagaac aatccttga
2161 tatttaaact aatctgctat taagaaattt agaagttgtat ctctgttatt aattggattt
2221 gtcctgaatt actccgtgg gacgctgaac aactcaagaa tacatggct gtgcttggca
2281 gcccctcccc atccctccca ccaccaccac cccccccccca acaaggccct atacctctg
2341 acctgtgagc cctgaagcta ttttaaggac ttctgttca gcataccgg tagtagctcc
2401 actaaaccat gatttctgga tgtctgttc tttagacctgc caacagctaa taagaacaat
2461 gtataaaat gtcagcttc attttaata tttgtgttca gttttttgt cgtgttttc
2521 taattaaaaa gaaaacgggc agtaaccctc ttcttatataa gcatttagtta atattaagg
2581 aaatcaaaca aatctaagcc aataactccca acaagcaagt tagatcttac ttctgtgtc
2641 gttgctgaaa tgtggcttt gcatgggtgg gtttcataaa acttttggc caagaggctt
2701 gtttagtatac atccatctgt ttagtcatca agttttgtat ttcacttaaa aaaaaataaa
2761 ccactagaca tcttttgcg aatgtcaaattt agtcacagtc taagtagcca aaaagtcaaa
2821 gcgtgttaaa cattgccaaa tgaaggaaag ggtgagctgc aaaggggatg gttcgaggtt
2881 cattccagtt gtgacccgag cgtccccaaa acctgggatg caaagacagt gattctgtcat
2941 atggcctgga aagacagggaa agccagtctc ctacaaaggaa gaatggaaga tcctggcctc
3001 taagtcatag accaaagtct gctgttag

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FIGURE 5A

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MSASLDTGDFQEFLKHGLTAIASAPGSETRHSPKREEQLREKRA
GLPDRHRRPIPARSLVMLPKVETEAPGLVRSHGEQQMPENMQVSQFKMVNYSYDED
LEELCPVCGDKVSGYHYGLLTCESCKGFFKRTVQNQKRYTCIENQNCQIDKTQRKRC
YCRFKKCIDVGMKLEAVRADMRRGGRNKFGPMYKRDRAKQQKKALIRANGLKLEAMS
QVIQAMPSDLTSAIQNIHSASKGLPLSHVALPPTDYDRSPFVTSPISMTPPHSSLHG
YQPYGHFPSRAIKSEYPDPYSSSPESMMGYSYMDGYQTNSPASIPHILELLKCEPDE
PQVQAKIMAYLQQEQSNRNRQEKLASFGLLCKMADQTLFSIVEWARSSIFFRELKVD
QMPLLQNCWSSELLILDHIYRQVAHGKEGTIFLVTGEHVDYSTIISHTEVAFNNLLSLA
QELVVRLRSLQFDQREFVCLKFLVLFSSDVKNLENLQLVEGVQEQQVNAALLDYTCNY
PQQTEKFGQLLRLPEIRAIISKQAEDYLYYKHVNGDVPYNNLLIEMLHAKRA

FIGURE 5B

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1 ttttgctcaa tgatttctgc tttaagccaa agaactgcct ataatttcac taagaatgtc
 61 ttctaattca gatactgggg atttacaaga gtccttaaag cacggactt cacctattgt
 121 gtctcaattt aaaatggta attactccta tcatgaagat ctgaaagagc tttgtcccg
 181 gtgtggagat aaagtgtctg ggtaccattt tgggctcctc acctgtgaaa gctgcaaggg
 241 atttttaag cgaacagtcc aaaataataa aaggtaacaca tgtatagaaa accagaactg
 301 ccaaattgac aaaacacaga gaaagcggt tccttactgt cgtttcaaa aatgtctaag
 361 tggtaatg aagctagaag ctgtaaggc cgaccgaatg cgtggaggaa ggaataagtt
 421 tggccaatg tacaagagag acagggccct gaagcaacag aaaaaagccc tcatccgac
 481 caatggactt aagctagaag ccatgtctca ggtgatccaa gctatgcct ctgacactgac
 541 catttcctct gcaattcaaa acatccactc tgcctccaaa ggcctacctc tgaaccatgc
 601 tgccttgccct cctacagact atgacagaag tcccttgc acatccccca ttagcatgac
 661 aatgccccct cacggcagcc tgcaaggta ccaaacatata ggcacttcc ctggccggc
 721 catcaagtct gagtacccag acccctatac cagctcaccc gagtcataa tgggctattc
 781 atatatggat agttaccaga cgagctctcc agcaagcatc ccacatctga tactgaaact
 841 ttgttgttggat gagccagatg agcctcaagt ccaggctaaa atcatggctt atttgcagca
 901 agagcaggct aaccgaagca agcacgaaaa gctgagcacc tttgggctta tggcaaaat
 961 ggcagatcaa actctttct ccattgtcga gtgggcccagg agtagtatct tcttcagaga
 1021 acttaagggtt gatgacccaaa tgaagctgct tcagaactgc tggagtgagc tcttaatcct
 1081 cgaccacatt taccgacaag tggtacatgg aaaggaagga tccatcttcc tggttactgg
 1141 gcaacaagtg gactattcca taatagcatc acaagccgaa gcccacccatca acaacccat
 1201 gagtcatgca caggagttt tggcaaaact tcgttctctc cagtttgc tttttttttt aacgagagtt
 1261 cgtatgtctg aaattttgg tgctctttag tttagatgtc aaaaaccttgg aaaaacttccaa
 1321 gctgttagaa ggtgtccagg aacaagtcaa tgccgcctt ctggactaca caatgtgtaa
 1381 ctacccgcag cagacagaga aatttggaca gctacttctt cgactacccg aaatccggc
 1441 catcagtatg caggctgaag aatacctcta ctacaaggcac ctgaacgggg atgtcccta
 1501 taataacctt ctcattgaaa tggatgtcga caaaagagca taagttacaa ccccttaggag
 1561 ctctgctttc aaaacaaaaa gagattgggg gagtggggag ggggaagaag aacaggaaga
 1621 aaaaaagtac tctgaactgc tccaaagcaac gctaattaaa aacttgcctt aaagatattt
 1681 aattaaaaaa ggcataataa tcaaataactt aatagcaaat aaatgtatgtc tcagggtatt
 1741 tgtattgcaa actgtgaatc aaaggcttca cagccccaga ggattccata taaaagacat
 1801 tgtaaggagt ggattgaact cacagatgga taccaacacg gtcagaagaa aaacggacag
 1861 aacggttctt gtatattaaa ctgatctcca ctatgaagaa atttaggaac taatcttgg
 1921 aattaggctt atacagcggtt ggatttgagc ttacaggatt cctccatggt aaagctgaac
 1981 tgaacaattt ctcagaatg catcagctgt acttacaata gcccctccctt cttccttga
 2041 agggccgagc acctctgccc tgggtcacc gaatctgtac taaggacctg tggcagcca
 2101 caccagtggt agtccacca aatcatgaac agcctaattt gatgtctgt gtcttagacc
 2161 tgcaaaacagc taataggaaa ttcttattat atgttagctt gccatattaa atatgttctg
 2221 aggttgttt tggatgtt tcatgtatgg aaaaaatgc aggcagtatc cctcatctt
 2281 tgtaagtgtt aattaaatatt aaggaaatg actacaaact ttcaaagcaa atgctccata
 2341 gctaaagcaa ctttagacctt atttctgcta ctgttgcga aatgtggctt tggcattgtt
 2401 ggatttcata aaaaatttctt ggcaggaagt ctgtttagta tacatcagtc tttttcatca
 2461 tccaaatggat tagttcattt aa

FIGURE 6A

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MSSNSDTGDLQESLKHLTPIVSQFKMVNSYDEDLEELCPVCG
DKVSGYHYGLLTCESCKGFFKRTVQNNKRYTCIENQNCQIDKTQRKRCPYCRFQKCLS
VGMKLEAVRADMRRGGRNKFGPMYKDRRALKQQKKALIRANGLKLEAMSQVIQAMPSD
LTIISSAIQNIHSASKGLPLNHAALPPTDYDRSPFVTSPISMTPPHGSLQGYQTYGHF
PSRAIKSEYPDPTSSPESIMGSYMDSYQTSSPASIPHLLKCEPDEPQVQAKI
MAYLQQEQANRSKHEKLSTFGLMCKMADQTLFSIVEWARSSIFFRELKVDDQMKLQN
CWSSELLILDHIYRQVVHGKEGSIFLVGTQQVDYSIIASQAGATLNNLMSHAQELVAKL
RSLQFDQREFVCLKFLVLFSLDVKNLENFQLVEGVQEQQVNAALLDYTMCNYPQQTEKF
GQLLLRLPEIRAISSMQAEEYLYYKHLNGDVPYNNLLIEMLHAKRA

FIGURE 6B

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Variant 1

655 tcagga
661 gggcccaatg taccagagct catattgcag ctgctgcaac tagagccaga ggaggaccag
721 gtgcgcgctc gcacatcggtgg ctgtctgcag gagccagcca aaagccgctc tgaccagcc
781 gcgcccttca gcctcctctc **gc**gaatggcc gaccagacct ttatctccat tgtcactgg
841 gcacgaaagg tgcattggctt taaggagctg gaggtggctg accagatgac actgctgca
901 aactcttgg a gcgagctgct ggtgttggac cacatctacc gccaggtcca gtacggcaag
961 gaagacagca tcctgctggg tactggacag gaggtggagc tgagcacagt ggctgtgcag
1021 gctggctccc tgctgcacag cctgggtctg cggggcccaag agtttagtgc cttagttgc
1081 gcactgcagc tggaccgcca ggagttcgct tgtctcaagt tcctcatcct cttcagcc
1141 gatgtgaaat tcctgaacaa ccacagcctc gtaaaggacg cccaggaaaa ggccaacgc
1201 gcccgttgg attacacacctt gtgtcactac ccacactgcg gggacaaatt ccagcagtt
1261 ctattgt**cg**c tgggtggaggt gcggggccctg agcatgcagg ccaaggagta cctgtaccac
1321 aagcatttgg gcaacgagat gccccgcaac aaccttctca ttgagatgct gcaggccaag
1381 cagacttqa

SG

GPNVPELILQ LLQLEPEEDQ VRARIVGCLQ EPAKSRSRDQP APFSLLSRMA DQTFISIVDW
ARRCMVFKEL EVADQMTLLQ NSWSELLVLD HIYRQVQYQK EDSILLVTGQ EVELSTVAVQ
AGSLLHSLVL RAQELVLQLH ALQLDRQEFV CLKFLILFSL DVKFLNNHSL VKDAQEKANA
ALLDYTILCHY PHCGDKFQQL LLSLVEVRAL SMQAKELYH KHLGNEMPRN NLLIEMLOAK QT

FIGURE 7A

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Variant 2

655 tcagga
661 gggcccaatg taccagagct catattgcag ctgctgcaac tagagccaga ggaggaccag
721 gtgcgcgctc gcatcgaaa ctgtctgcag gagccagcca aaagccgctc tgaccagcca
781 gcgccttca gcctcctctg cagaatggcc gaccagactt ttatctccat tgtcactgg
841 gcacgaaggt gcatggtctt taaggagctg gaggtggctg accagatgac actgctgca
901 aacttttgg a gcgagctgct ggtgttggac cacatctacc gccaggtcca gtacgcaag
961 gaagacagca tcctgcttgt tactggacag gaggtggagc tgagcacagt ggctgtgcag
1021 gctggctccc tgctgcacag cctggctg cggggccaa agtttagtgc ccagttgc
1081 gcaactgcagc tggaccgcca ggagttcg tgc tgc tca a g t t c c t c t c t c t
1141 gatgtgaaat tcctgaacaa ccacagcctc gtaaaggacg cccaggaaaa ggccaacgct
1201 gccctgttgg attacacatt gtgtcactac ccacactgcg gggacaaatt ccagcagttg
1261 ctattgtcg tggggaggt gcggccctg agcatgcagg ccaaggagta cctgttaccac
1321 aagcatttgg gcaacgagat gcccccaac aacttctca ttgagatgct gcaggccaag
1381 cagacttga

SG

GPNVPELILQ LLQLEPEEDQ VRARIVGCLQ EPAKSRSRSDQP APFSLLCRMA
DQTFISIVDW ARRCMVFKEL EVADQMTLLQ NSWSELLVLD HIYRQVQYQK
EDSILLVTGQ EVELSTVAVQ AGSLLHSLVL RAQELVILQLH ALQLDRQEFV
CLKFLILFSL DVKFLNNHSL VKDAQEKANA ALLDYTLCHY PHCGDKFQQL
LLSLVEVRAL SMQAKELYH KHLGNEMPRN NLLIEMLQAK QT

FIGURE 7B

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Variant 3

655 tcagga
661 gggcccaatg taccagagct catattgcag ctgctgcaac tagagccaga ggaggaccag
721 gtgcgcgctc gcacatcggtt ctgtctgcag gagccagcca aaagccgctc tgaccagcca
781 gcgccctca gcctcctctg cagaatggcc gaccagacct ttatctccat tgtcgactgg
841 gcacgaaggt gcatggtctt taaggagctg gaggtggctg accagatgac actgctgcag
901 aactgttggc gcgagctgct ggtgttggac cacatctacc gccaggtcca gtacggcaag
961 gaagacagca tcctgctggt tactggacag gaggtggagc tgagcacagt ggctgtgcag
1021 gctggctccc tgctgcacag cctgggtctg cggggccaaag agtttagtgc ccagttgcatt
1081 gcactgcagc tggaccgcctt ggagttcgct tgcgtctcaagt tcctcatcct cttcagccct
1141 gatgtgaaat tcctgaacaa ccacagcctc gtaaaggacg cccaggaaaa ggccaacgc
1201 gcccgttgg attacacctt gagcactac ccacactccg gggacaaatt ccagcagttg
1261 ctattgtgcc tgggtggaggt gcggggccctg agcatgcagg ccaaggagta cctgttaccac
1321 aagcatttgg gcaacgagat gccccgcaac aaccttctca ttgagatgct gcaggccaaag
1381 caqacttqa

SG

GPNVPELILQ LLQLEPEEDQ VRARIVGCLQ EPAKSRSDQP APFSLLCRMA DQTFISIVDW
ARRCMVFKEL EVADQMTLLQ NCWSELLVLD HIYRQVQYGK EDSILLVTGQ EVELSTVAVQ
AGSLLHSLVL RAQELVLQLH ALQLDRQEJV CLKFLILFSL DVKFLNNHSL VKDAQEKANA
ALLDYTL~~SHY~~ PH~~S~~GDKFOQL LLCLVEVRAL SMOAKELYLYH KHLGNEMPRN NLLIEMLOAK QT

FIGURE 7C

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Variant 4

655 tcagga
661 gggcccaatg taccagagct catattgcag ctgctgcaac tagagccaga ggaggaccag
721 gtgcgcgctc gcatcgtggg ctgtctgcag gagccagcca aaagccgctc tgaccagcca
781 gcgcccttca gcctcctctg cagaatggcc gaccagacct ttatctccat tgtcgactgg
841 gcacgaagggt gcatggtctt taaggagctg gaggtggctg accagatgac actgctgcaaa
901 aactcttggaa gcgagctgct ggtgttggac cacatctacc gccaggtcca gtacggcaag
961 gaagacagca tcctgctggta tactggacag gaggtggagc tgagcacagt ggctgtgcag
1021 gctggctccc tgctgcacag cctggctg cgggcccaag agttagtgct ccagttgcatt
1081 gcactgcagc tggaccgcca ggagttcgct tgtctcaagt tcctcatcct cttcagccctc
1141 gatgtgaaat tcctgaacaa ccacaggctc gtaaaaggacg cccagaaaaa ggccaacgct
1201 gcccgttgg attacacctt gagccactac ccacactccg gggacaaatt ccagcagttg
1261 ctattgtcg tggtggaggt gcggggccctg agcatgcagg ccaaggagta cctgtaccac
1321 aagcatttgg gcaacgagat gccccgcaac aacccttctca ttgagatgct gcaggccaag
1381 cagacttga

SG

GPNVPELILQ LLQLEPEEDQ VRARIVGCLQ EPAKSRSRSDQP APPSILLCRMA DQTFISIVDW
ARRCMVFKEL EVADQMTLLQ NSWSELLVLD HIYRQVQYQK EDSILLVTGQ EVELSTVAVQ
AGSLLHSLVL RAQELVLQLH ALQOLDRQEFLV CLKFLILFSL DVKFLNNHSL VKDAQEKANA
ALLDYTL SHY PHSGDKFQQL LLSLVEVRAL SMQAKELYLH KHLGNEMPRN NLLIEMLQAK QT

FIGURE 7D

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A**Expression & Induction**

Expression in vector PBH4 BL21(De3)plys-S
6xHis-TCS-SF-1 (aa 177-462) Growth at 25°C for
o/n, IPTG induction at 0.2 OD for 6-8hr (~25mg/liter)

Talon Chromatography

Freeze-Thaw in 0.08% Triton X,
Lysozyme/DNase Centrifuge @50,000 g
Supernatant - Talon™ chromatography
Step elution with 80mM imidazole

TEV Cleavage

Cleavage with TEV protease (1:200)
at 30°C with dialysis against 10mM BME, Talon™ chromatography. Process flowthrough

Modification of Cysteines

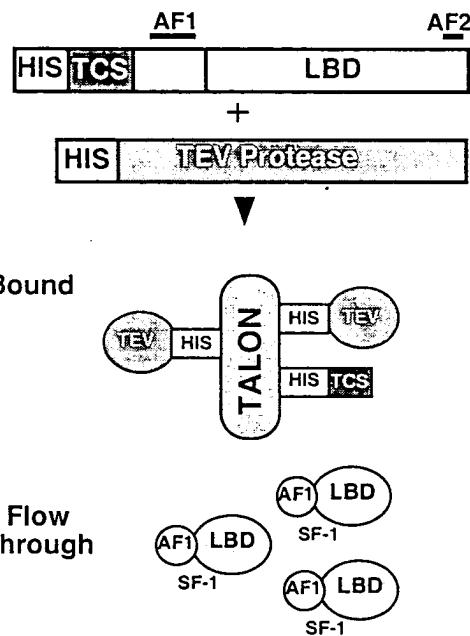
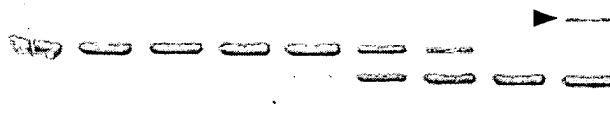
Carboxymethylation of homocysteine sulfhydryls
by treatment with 100mM iodoacetate o/n

Ion Exchange Chromatography

Quench by Poros-Q (cation exchange) at pH 8.5,
Step gradient 150mM NaCl to elute

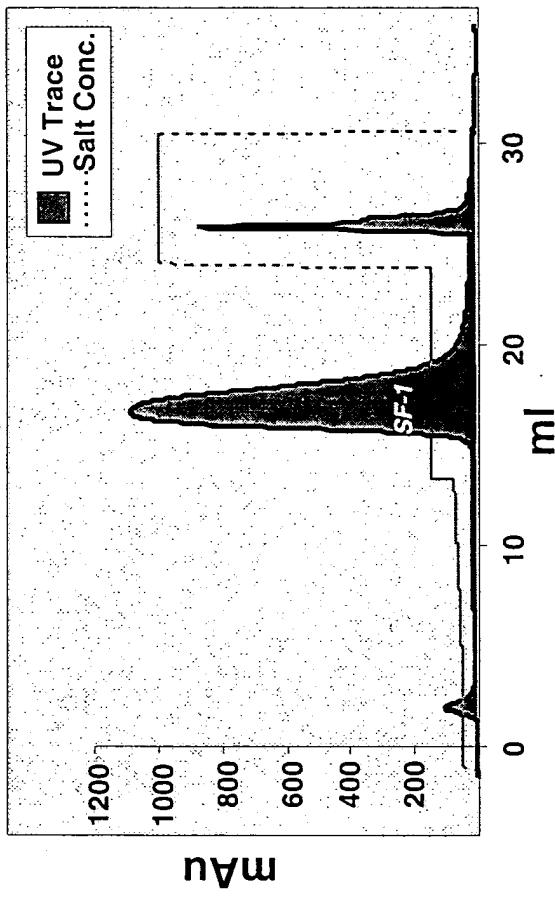
Gel Filtration

FPLC with Superdex 200 Column Buffer Exchange
freeze or use following ultracentrifugation

B**C****22kDa Protein X**

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POROS Q Column



Superdex 200 Column

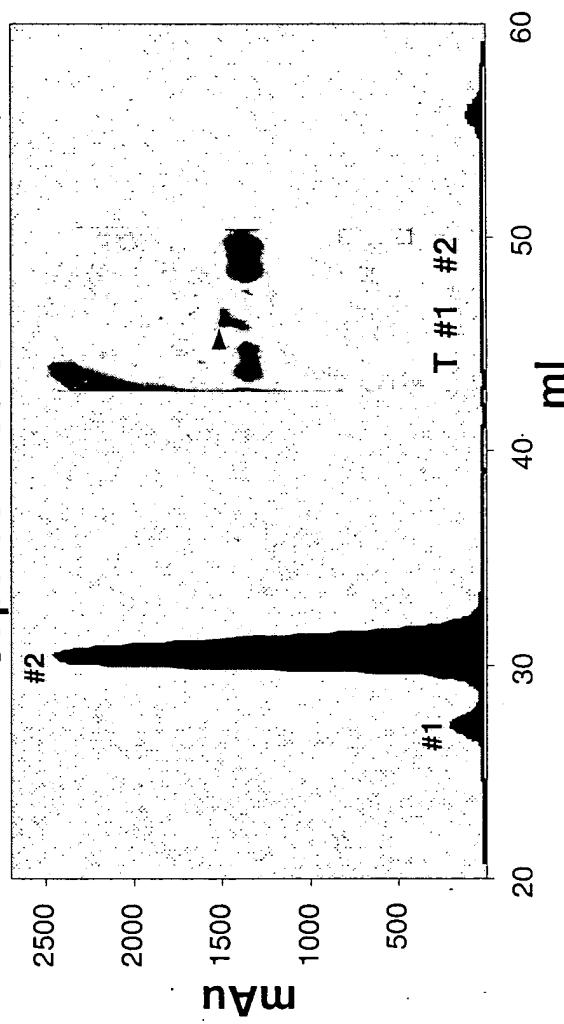


FIGURE 9

Mass Spectrum of SF-1 (Wildtype)

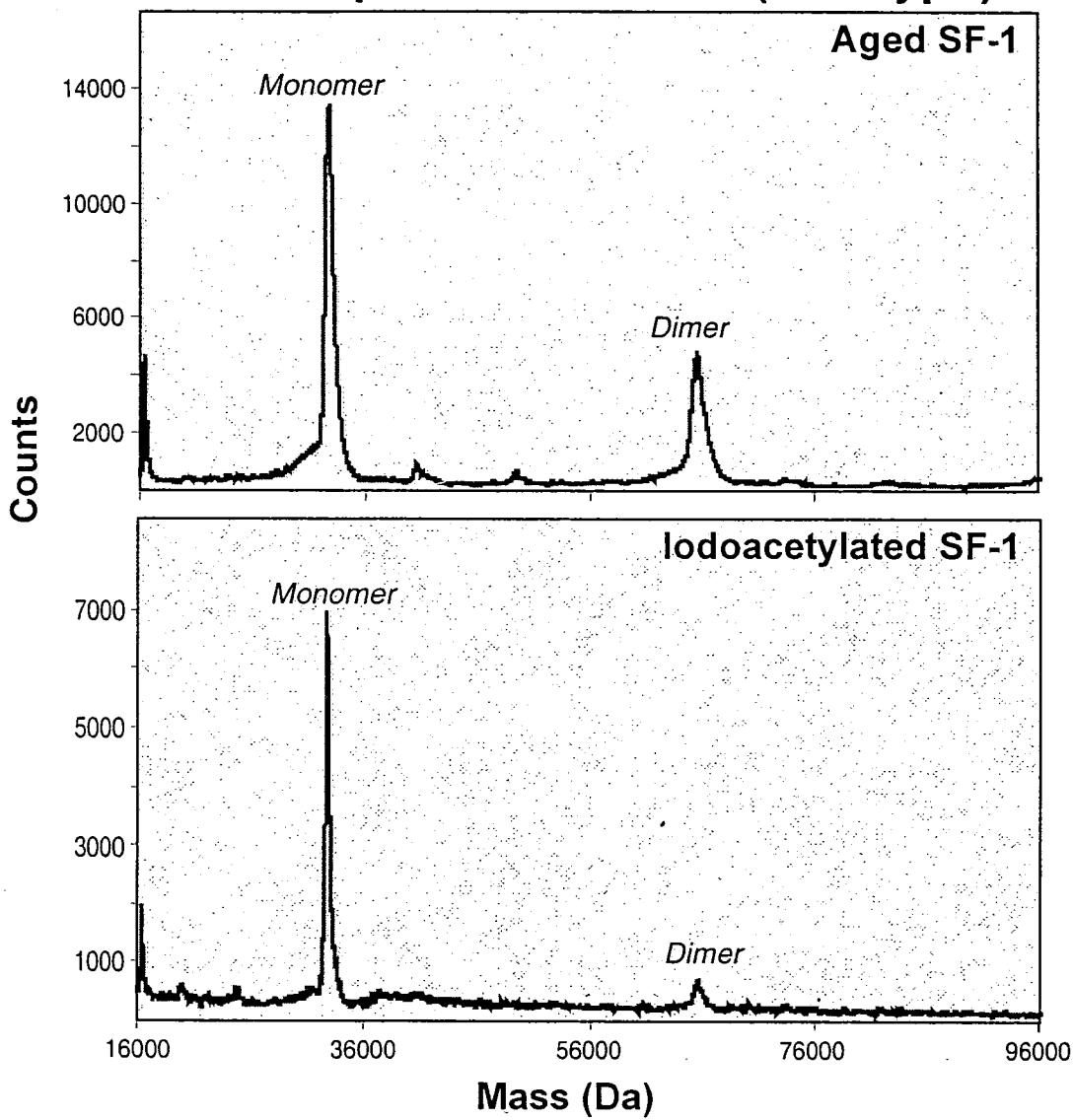


FIGURE 10

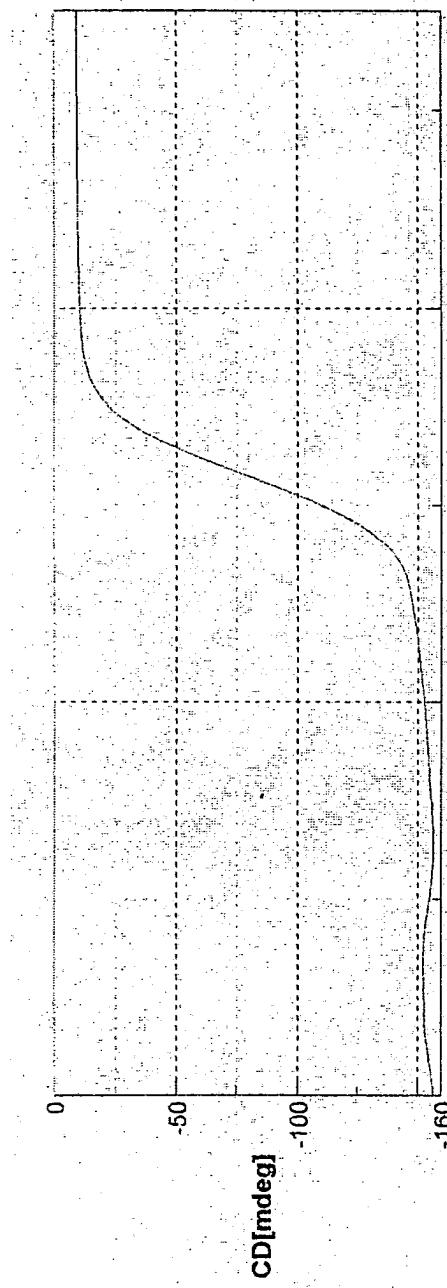


FIGURE 11

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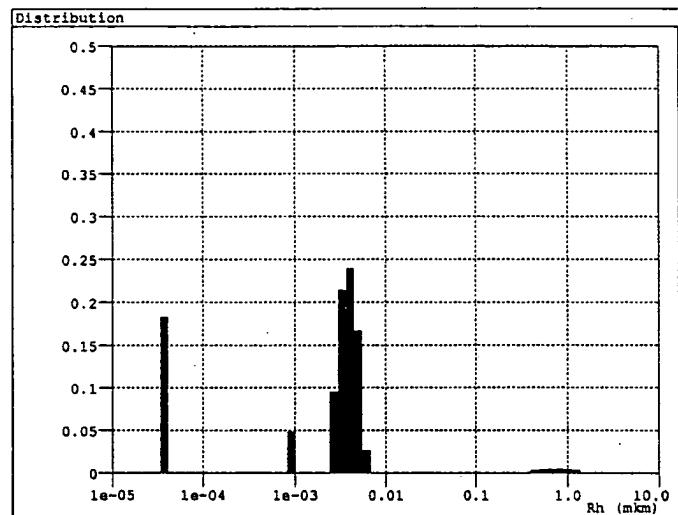


FIGURE 12A

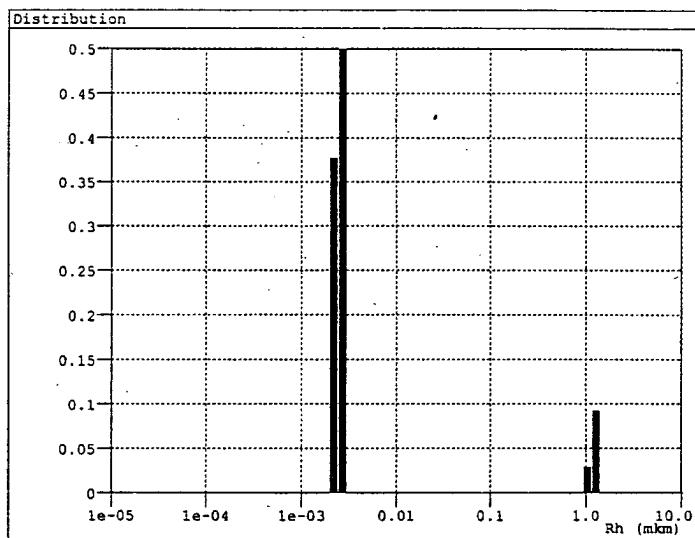


FIGURE 12B

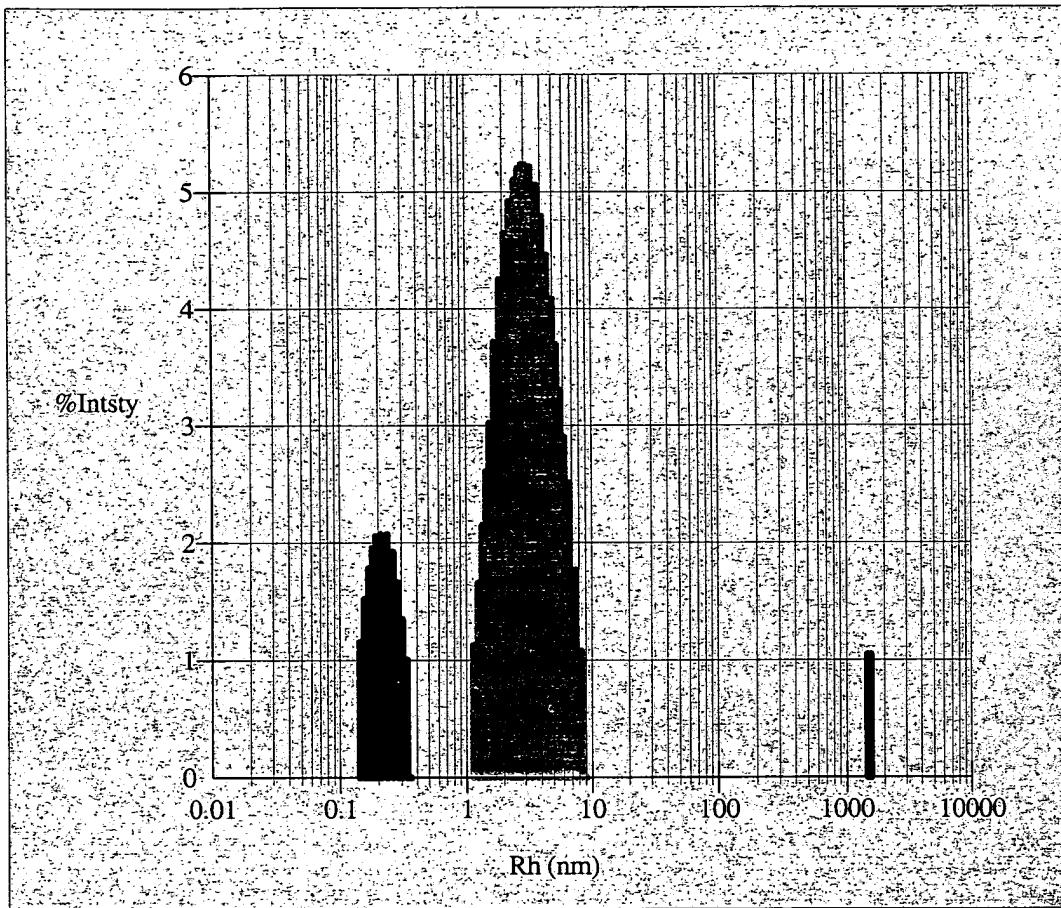


FIGURE 12C

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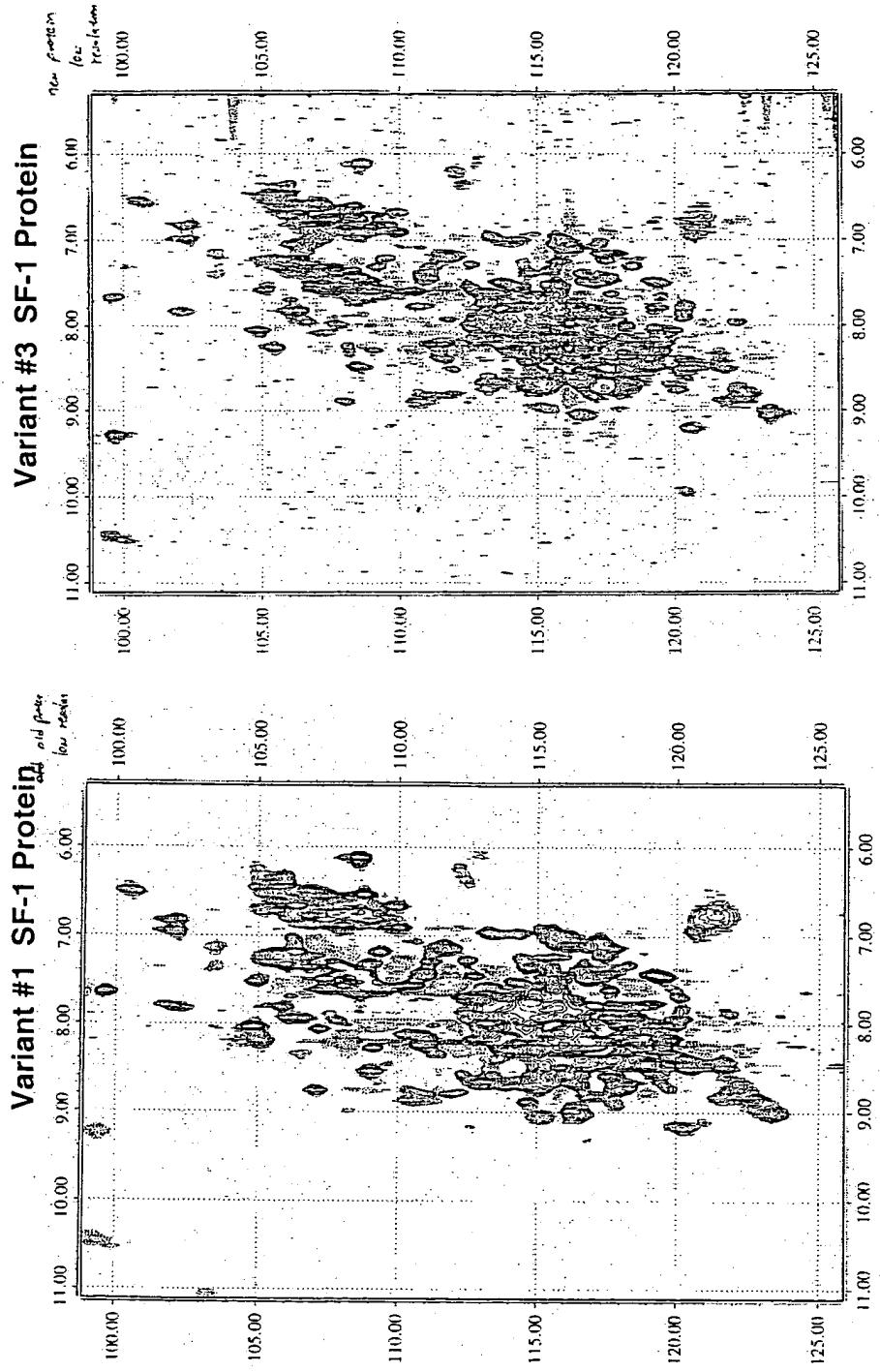


FIGURE 13

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Variant # 1

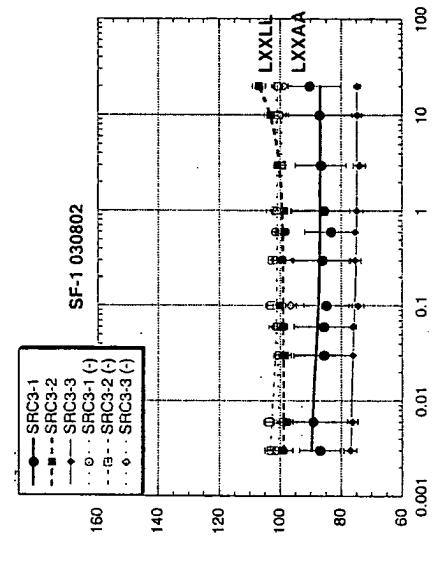
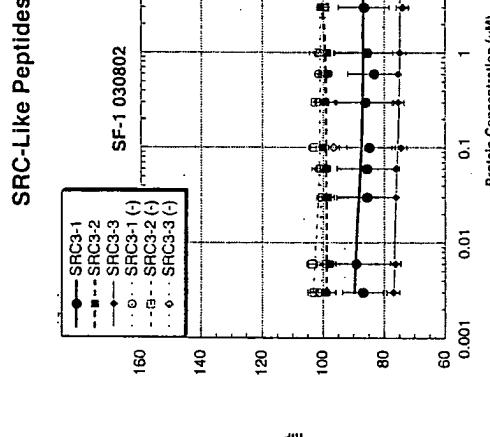
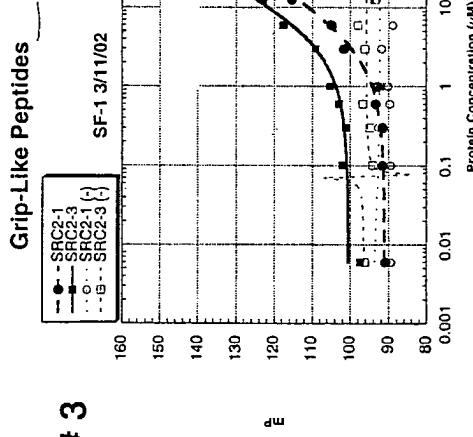
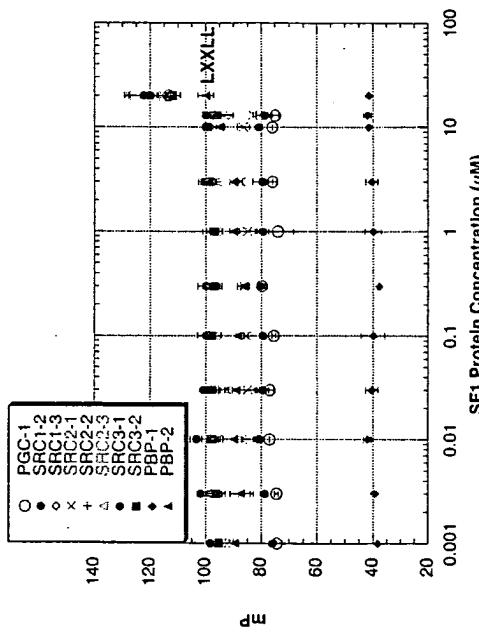


FIGURE 14